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SQUIRES, ELIZA A	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/814,852	FAVA ET AL.	
	Examiner	Art Unit	
	Eliza Squires	4156	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 March 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-33* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *31 March 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/30/08, 9/28/07, 6/4/07, 6/1/07, 3/31/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This communication is in response to the application filed on 31 March 2004. Claims 1-33 are pending.

Requirement for Information under 37 CFR 1.105

Applicant and the assignee of this application are required under 37 CFR 1.105 to provide the following information that the examiner has determined is reasonably necessary to the examination of this application.

In response to this requirement, please provide the title, citation and copy of each publication, text, or relevant material, that any of the applicants relied upon to develop the disclosed subject matter that describes the applicant's invention, particularly as to developing the formulas of claims 14 and 15. For each document provided, please provide a concise explanation of the reliance placed on that publication in the development of the disclosed subject matter.

In responding to those requirements that require copies of documents, where the document is a bound text or a single article over 50 pages, the requirement may be met by providing copies of those pages that provide the particular subject matter indicated in the requirement, or where such subject matter is not indicated, the subject matter found in applicant's disclosure.

The fee and certification requirements of 37 CFR 1.97 are waived for those documents submitted in reply to this requirement. This waiver extends only to those documents within the scope of this requirement under 37 CFR 1.105 that are included in the applicant's first complete communication responding to this requirement. Any

supplemental replies subsequent to the first communication responding to this requirement and any information disclosures beyond the scope of this requirement under 37 CFR 1.105 are subject to the fee and certification requirements of 37 CFR 1.97.

The applicant is reminded that the reply to this requirement must be made with candor and good faith under 37 CFR 1.56. Where the applicant does not have or cannot readily obtain an item of required information, a statement that the item is unknown or cannot be readily obtained may be accepted as a complete reply to the requirement for that item.

This requirement is an attachment of the enclosed Office action. A complete reply to the enclosed Office action must include a complete reply to this requirement. The time period for reply to this requirement coincides with the time period for reply to the enclosed Office action.

Examiner also would like to call to attention an article “The Problem of the Placebo Response in Clinical Trials for Psychiatric Disorders: Culprits, Possible Remedies, and a Novel Study Design Approach", while not considered prior art, it appears to have been written by the two inventors of this application as well as two additional authors. This article contains the formulas of claims 14 and 15 which are the subject of this requirement.

Claim Objections

1. Claim 14-16 are objected to as being dependent upon a rejected base claim, but would be allowable if:

a. they are rewritten in independent form including all of the limitations of the base claim and any intervening claims;

b. any deficiencies under 35 U.S.C 101, 112, etc. are overcome.

Claim Rejections - 35 USC § 101

2. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

3. **Claims 1-33** are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

a. **With respect to claims 1-24**, a method, as directed to by the claim 1, must be substantially tied to another statutory class within the body of the claims. Claims 2-24 fail to rectify this deficiency and are therefore rejected for the same reasons. In order for a method to be considered a "process" under 35 U.S.C. 101, a claimed process must either: (1) be tied to another statutory class (such as a particular apparatus) or (2) transform underlying subject matter (such as an article or materials). *Diamond v. Diehr*, 450 U.S. 175, 184 (1981); *Parker v. Flook*, 437 U.S. 584, 588 n.9 (1978); *Gottschalk v. Benson*, 409 U.S. 63, 70 (1972). If neither of these requirements is met by the claim, the method is not a patent eligible process under 35 U.S.C. 101 and is nonstatutory subject matter. The claims recite no substantive tie to another statutory class in the body of the claims and are therefore rejected.

b. **With respect to claims 25-33,** the independent claims, 25 and 29, are broad as to read on both statutory and non-statutory classes. These claims may refer to software per se which is non statutory under 35 U.S.C. 101. Claims to computer-related inventions that are clearly nonstatutory fall into the same general categories as nonstatutory claims in other arts, namely natural phenomena such as magnetism, and abstract ideas or laws of nature which constitute "descriptive material." Abstract ideas, Warmerdam, 33 F.3d at 1360, 31 USPQ2d at 1759, or the mere manipulation of abstract ideas, Schrader, 22 F.3d at 292-93, 30 USPQ2d at 1457-58, are not patentable. Descriptive material can be characterized as either "functional descriptive material" or "nonfunctional descriptive material." In this context, "functional descriptive material" consists of data structures and computer programs which impart functionality when employed as a computer component. (The definition of "data structure" is "a physical or logical relationship among data elements, designed to support specific data manipulation functions." The New IEEE Standard Dictionary of Electrical and Electronics Terms 308 (5th ed. 1993).) "Nonfunctional descriptive material" includes but is not limited to music, literary works and a compilation or mere arrangement of data. Both types of "descriptive material" are nonstatutory when claimed as descriptive material per se. Warmerdam, 33 F.3d at 1360, 31 USPQ2d at 1759. Claims 26-28 and 30-33 fail to remedy the deficiency of the claims from which they are dependant and are rejected for the same reasons

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. **Claims 25-28** are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The structure of a "randomizer" and an "analyzer" are not disclosed in the specification and one skilled in the art would be unable to reproduce such features as it is unclear what it may comprise.

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. **Claim 15, 19 and 25-29** are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. **Claim 15 and 19** recite the variable "a" within the formula; the variable "a" is not defined by claims which render the claims indefinite.

b. **Claim 25-28** are vague and indefinite as it is unclear as to what a randomizer or an analyzer may comprise, and one of ordinary skill in the art at

the time of the invention would not be reasonably apprised of the scope of the invention.

8. **Claims 7-9** are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. **Claim 7-9** recite the limitation "the treatment time" in line 1 of each claim. There is insufficient antecedent basis for this limitation in the claim.

9. **Claims 29-33** are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. **As to claim 29, 32, and 33,** claim elements of claim 29 “means for randomizing”, “means for performing a first phase”, “means for determining”, “means for performing a second phase”, and “means for analyzing” is a means (or step) plus function limitation that invokes 35 U.S.C. 112, sixth paragraph. However, the written description fails to disclose the corresponding structure, material, or acts for the claimed function. Claims 32 and 33 are dependant on the rejected claim and fail to remedy the deficiency and are therefore rejected for the same reasons.

b. **As to claim 30,** claim element “means for storing” is a means (or step) plus function limitation that invokes 35 U.S.C. 112, sixth paragraph. However, the written description fails to disclose the corresponding structure, material, or acts for the claimed function.

c. **As to claim 31,** claim element "means for determining an effectiveness" is a means (or step) plus function limitation that invokes 35 U.S.C. 112, sixth paragraph. However, the written description fails to disclose the corresponding structure, material, or acts for the claimed function.

Applicant is required to:

(a) Amend the claim so that the claim limitation will no longer be a means (or step) plus function limitation under 35 U.S.C. 112, sixth paragraph; or

(b) Amend the written description of the specification such that it expressly recites what structure, material, or acts perform the claimed function without introducing any new matter (35 U.S.C. 132(a)).

If applicant is of the opinion that the written description of the specification already implicitly or inherently discloses the corresponding structure, material, or acts so that one of ordinary skill in the art would recognize what structure, material, or acts perform the claimed function, applicant is required to clarify the record by either:

(a) Amending the written description of the specification such that it expressly recites the corresponding structure, material, or acts for performing the claimed function and clearly links or associates the structure, material, or acts to the claimed function, without introducing any new matter (35 U.S.C. 132(a)); or

(b) Stating on the record what the corresponding structure, material, or acts, which are implicitly or inherently set forth in the written description of the specification, perform the claimed function. For more information, see 37 CFR 1.75(d) and MPEP 2181 and 608.01(o).

Claim Rejections - 35 USC § 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11. **Claims 1, 6-7, 9-12, 17-20, 29, and 31-33** are rejected under 35 U.S.C. 102(b) as being anticipated by "The Double-Blind Variable Placebo Lead-in Period: Results From Two Antidepressant Clinical Trials" by *Faries et al.*

12. **As to claim 1,** *Faries* discloses a method of performing a clinical trial comprising:

randomizing study participants into a plurality of treatment groups (page 564, right column);

performing a first phase of testing, said first phase of testing including administering an active treatment to a first group of said plurality of treatment groups, and administering a placebo to a remainder of said treatment groups (page 564 right column and figure 2);

determining whether each participant in each of said treatments groups is a responder or a non-responder (page 564, right column and figures 2 and 4);

performing a second phase of testing, said second phase of testing including administering said placebo to at least one non-responder in at least one group, and administering said active treatment to at least one non-responder in at least one group (page 564, right column, figures 2 and 4, and abstract); and

analyzing data from at least one of said first phase of testing and from said second phase of testing (Results Section).

13. **As to claim 6,** see the discussion of claim 1 above, *Faries* additionally discloses the method wherein the clinical trial comprises a double-blind clinical trial (page 564, Methods section).

14. **As to claim 7,** see the discussion of claim 1 above, *Faries* further discloses the method wherein the treatment time for each of said plurality of groups is the same (figure 2 and page 563).

15. **With respect to claim 9,** see the discussion of claim 1 above, additionally, *Faries* further discloses the method wherein the treatment time for the first phase is different than the treatment time for the second phase (Figure 2 and page 564 Methods section).

16. **As to claim 10,** see the discussion of claim 1 above, *Faries* additionally discloses the method wherein said active treatment corresponds to a drug treatment (page 564 Methods section).

17. **As to claim 11,** see the discussion of claim 1 above, *Faries* further discloses the method wherein said analyzing comprises determining an effect of active treatment (figure 3, table 1, and page 565 results section).

18. **As to claim 12,** see the discussion of claim 1 above, additionally, *Faries* further discloses the method wherein said analyzing comprises determining a placebo response rate (figure 3, table 1, and page 565 results section).

19. **As to claim 17,** see the discussion of claim 1 above, *Faries* additionally discloses the method wherein said randomizing study participants into a plurality of treatment groups comprises randomizing said study participants into a first treatment group and a second treatment group (page 564 right column and figure 2, where group 1 is randomized to a 0 week placebo lead in and group 2 is randomized to a 1 week double blind placebo lead in).

20. **As to claim 18,** see the discussion of claim 1 above, *Faries* additionally discloses the method further comprising randomizing said study participants into a third treatment group (page 564 right column and figure 2, where group 1 is randomized to a 1 week placebo lead in, group 2 is randomized to a 0 week placebo lead in again randomized to placebo, and group 3 is randomized to a 0 week double blind placebo lead in again randomized to fluoxetine).

21. **As to claim 19,** see the discussion of claim 1 above, *Faries* additionally discloses the method wherein said administering a placebo to a remainder of said treatment groups comprises administering said placebo to said second group of said plurality of treatment groups and administering said placebo to said third group of said plurality of treatment groups (page 564 right column and figure 2).

22. **As to claim 20,** see the discussion of claim 1 above, *Faries* additionally discloses the method wherein said second phase of testing comprises administering said placebo to non-responders in said first group, administering said active treatment to non- responders in said second group, and administering said placebo to non-

responders in said third group (page 564 right column wherein each group is comprised of responders and non-responders [figure 4]).

23. **With respect to claim 29,** *Faries* discloses a system for performing a clinical trial comprising:

means for randomizing study participants into a plurality of treatment groups (page 564 right column);

means for performing a first phase of testing, said first phase of testing including administering an active treatment to a first group of said plurality of treatment groups and administering a placebo to a remainder of said treatment groups (page 564 right column and figure 2 and figure 4);

means for determining whether each subject in each of said treatments groups is a responder or a non-responder (page 564 right column and page 565 left column);

means for performing a second phase of testing, said second phase of testing including administering said placebo to non-responders in said first group, administering said active treatment to at least one non-responder in said remainder of treatment groups, and administering said placebo to at least one non-responders in said remainder of treatment group (page 564 right column and figure 2 and figure 4); and

means for analyzing data from at least one of said first phase of testing and from said second phase of testing (page 567 right column and figure 4).

24. **As to claim 31**, see the discussion of claim 29, additionally, *Faries* discloses the system wherein said means for analyzing comprises means for determining an effectiveness of said active treatment (page 567 right column and figure 4).

25. **As to claim 32,** see the discussion of claim 29, additionally, *Faries* the system wherein said plurality of groups comprises a first treatment group and a second treatment group (page 564 right column and figure 2, where group 1 is randomized to a 0 week placebo lead in and group 2 is randomized to a 1 week double blind placebo lead in).

26. **As to claim 33,** see the discussion of claim 29, additionally, *Faries* discloses the system wherein said plurality of groups comprises a first treatment group, a second treatment group and a third treatment group (page 564 right column and figure 2, where group 1 is randomized to a 1 week placebo lead in, group 2 is randomized to a 0 week placebo lead in again randomized to placebo, and group 3 is randomized to a 0 week double blind placebo lead in again randomized to fluoxetine).

Claim Rejections - 35 USC § 103

27. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

28. **Claims 2, 3, 5, 23** are rejected under 35 U.S.C. 103(a) as being unpatentable over *Faries* in view of "A Randomized, Controled Trial of Maintenance Interferon Therapy for Patients with Chronic Hepatitis C Virus and Persistent Viremia" by *Shiffman et al*.

29. **As to claim 2,** *Faries* teaches the method of claim 1 as noted above but does not teach that treatment is discontinued for responders. In the same field of endeavor, *Shiffman* discloses the method further comprising discontinuing treatment for responders in at least one of said plurality of groups (page 2, paragraph 1 and figure 1).

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the phased testing utilizing placebo trials disclosed by *Faries* with the use of a process by which trial participants are entered into discontinued treatment as taught by *Shiffman* because it would permit the conductors of a clinical trial to evaluate the effect of maintenance of a drug or therapy as compared with its discontinued use (*Shiffman;* abstract).

30. **As to claim 3,** *Faries* teaches the method of claim 1 as noted above but does not teach that responders enter open continuation therapy. In the same field of

endeavor, *Shiffman* discloses entering open continuation therapy for responders in at least one of said plurality of groups (page 2, paragraph 1 and figure 1).

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the phased testing utilizing placebo trials disclosed by *Faries* with the use of a process by which trial participants are entered into continued therapy as taught by *Shiffman* because it would permit the conductors of a clinical trial to evaluate the effect of maintenance of a drug or therapy as compared with its discontinued use (*Shiffman;* abstract).

31. **As to claim 5,** *Faries* teaches the method of claim 1 as noted above but does not explicitly teach that at least two of the groups have a different number of study participants. The Examiner asserts, however, that such features are old and well known in the art and would be readily apparent to one of ordinary skill in the art. An example of this use is disclosed within the *Shiffman* reference, wherein the method comprises at least two of said treatment groups have a different number of study participants (page 1, Methods section).

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the phased testing utilizing placebo trials disclosed by *Faries* with the use of treatment groups with different sizes as taught by *Shiffman* since a field of participants may be odd. In order to create the greatest amount of data by not precluding an eligible participant in the study, the odd participant would be assigned to a group from a field comprising an even number of members thereby causing the number in each group to be unequal.

32. **As to claim 23,** see the discussion of claims 1 and 19, additionally, *Faries* discloses that there are three treatments groups. However, *Faries* does not explicitly disclose that two of the three has a different number participants (page 564 right column and figure 2, where group 1 is randomized to a 1 week placebo lead in, group 2 is randomized to a 0 week placebo lead in again randomized to placebo, and group 3 is randomized to a 0 week double blind placebo lead in again randomized to fluoxetine).

Shiffman discloses that two treatment groups have different numbers of study participants (page 1, Methods section).

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the phased testing utilizing placebo trials disclosed by *Faries* with the use of treatment groups with different sizes as taught by *Shiffman* since a field of participants may be odd. In order to create the greatest amount of data by not precluding an eligible participant in the study, the odd participant would be assigned to a group from a field comprising an even number of members thereby causing the number in each group to be unequal.

33. **Claims 4 and 22** are rejected under 35 U.S.C. 103(a) as being unpatentable over *Faries* in view of "Long-Term Effects of Glucosamine Sulphate on Osteoarthritis Progression: A Randomized, Placebo-Controlled Clinical Trial" by *Reginster et al.*

34. **As to claim 4,** *Faries* teaches the method of claim 1 as noted above but does not teach that treatment groups have the same number of participants The Examiner asserts, however, that such features are old and well known in the art and would be readily apparent to one of ordinary skill in the art. An example of this use is disclosed within the *Reginster* reference wherein said treatments groups have the same number of study participants (page 253, Results section wherein the placebo group and the glucosamine sulphate group each had 106 participants).

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the phased testing utilizing placebo trials disclosed by *Faries* with the use of treatment groups of the same size as taught by *Reginster* since the use of equally distributed participants in multiple groups will yield equally representitive statistics between the groups.

35. **As to claim 22,** see the discussion of claims 1 and 19, additionally, *Faries* further discloses that there are three treatment groups (page 564 right column and figure 2, where group 1 is randomized to a 1 week placebo lead in, group 2 is randomized to a 0 week placebo lead in again randomized to placebo, and group 3 is randomized to a 0 week double blind placebo lead in again randomized to fluoxetine).

However, *Faries* does not disclose that two of the groups have the same number of participants. *Reginster* discloses a system where two treatment groups have the

same number of study participants (page 253, Results section wherein the placebo group and the glucosamine sulphate group each had 106 participants).

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the phased testing utilizing placebo trials disclosed by *Faries* with the use of treatment groups of the same size as taught by *Reginster* since the use of equally distributed participants in multiple groups will yield equally representative statistics between the groups.

37. **Claim 8** is rejected under 35 U.S.C. 103(a) as being unpatentable over *Faries* in view of "A Randomized Trial of Itraconazole in Allergic Bronchopulmonary Aspergillosis" by *Stevens et al.*

38. **As to claim 8,** *Faries* teaches the method of claim 1 as noted above but does not teach that the treatment time for the first phase and the second phase is the same. In the same field of endeavor, *Stevens* discloses the method wherein the treatment time for the first phase and the second phase is the same (page 757, Study Design section).

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the phased testing utilizing placebo trials disclosed by *Faries* with the use of the same treatment time of different phases so that the conductor of the clinical trial would be able to evaluate a non-time dependant variable effectively, such as *Stevens* evaluation of response to a blinded and non-blinded trial (*Stevens;* Abstract).

39. **Claim 13** is rejected under 35 U.S.C. 103(a) as being unpatentable over *Faries* in view of "Development of a Multiple Sclerosis Functional Composite as a Clinical Trial Outcome Measure" by *Cutter et al.*

40. **As to claim 13,** see the discussion of claims 1 and 11 above, additionally *Faries* teaches discloses the method wherein said determining an effect of active treatment is assessed (figure 3, table 1, and page 565 results section).

Faries does not explicitly teach that it assessed using a z-score.

However, *Cutter* teaches a known technique wherein said determining a progression of a patient's physical state is assessed using a z-score (pages 874 and 875 Creation of a Z-Score section and page 875 Quantitative Composites section). This known technique is applicable to the method of *Faries* as they both share characteristics and capabilities, namely, they are directed towards methods of conducting and evaluating clinical trials

One of ordinary skill in the art would have recognized that applying the known technique of *Cutter* would have yielded predictable results and resulted in an improved system. *Cutter* teaches that the use of a Z-Score is a common statistical approach and useful when making metrics from different tests comparable (*Cutter*; page 874 right column, Creation of a Z-Score section).

41. **Claim 21** is rejected under 35 U.S.C. 103(a) as being unpatentable over *Faries* in view of "Traditional and Alternative Research Designs and Methods in Clinical Pediatric Psychopharmacology" by *Fava.*

42. **As to claim 21,** see the discussion of claims 1 and 19 above, however, *Faries* does not explicitly teach entering open continuation therapy for responders in each of the three groups. *Fava* discloses the method of further comprising entering open continuation therapy for responders in said first group, responders in said second group and responders in said third group (page 1294 left column, figure 7 B, and page 1295 wherein a test group is comprised of responders and non responders).

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the phased testing utilizing placebo trials disclosed by *Faries* with the use of a process by which trial participants are entered into continued therapy as taught by *Fava* since the combination would allow researchers to obtain "...a "true" drug response" demonstrated by "a persistent stable pattern of improvement" (*Fava* page 1294).

45. **Claim 24** is rejected under 35 U.S.C. 103(a) as being unpatentable over *Faries* in view of "Cyclandelate in the Prophylaxis of Migraine: A Randomized, Parallel, Double-Blind Study in Comparison With Placebo and Propranolol" by *Diener et al.*

46. **As to claim 24,** see the discussion of claims 1 and 19, however, *Faries* does not explicitly teach that the three treatment groups are randomized according to a ratio of 1-2a for the first group, a for the second, and a for the third. *Diener* discloses the use of a 3:2:3 randomization fraction for a controlled, unbalanced, clinical trial (abstract). Since the use unbalanced clinical trials is well known in the art as demonstrated by the *Diener* reference it would have been obvious to try, by one of ordinary skill in the art at the time of the invention, since there are a finite number of ratios to be used in a trial population and merely claiming use of one possible ratio does not patentably distinguish the claimed invention from the prior art. In addition, applicant has failed to demonstrate the criticality of the claimed ratios versus other possible ratios.

47. **Claims 25, 26-28, and 30** are rejected under 35 U.S.C. 103(a) as being unpatentable over *Faries* in view of U.S. Patent 5,991,731 to *Colon et al.*

48. **As to claim 25,** *Colon* discloses a system for performing a clinical trial comprising:

a database including a listing of identified study participants for the clinical trial (column 5 lines 25-35);

a first randomizer providing a plurality of randomized groups of study participants from said database of identified participants (column 5 lines 35-63);

However, *Colon* does not explicitly teach a system containing multiple groups of participants that when given treatment result in responders and non-responders. *Faries* discloses:

a first pool of study participants wherein a first group of randomized study participants selected from said first pool of study participants receive a first treatment and a remainder of said groups of randomized study participants of said first pool of study participants receive a second treatment, administration of said first treatment resulting in responders to said first treatment and non-responders to said first treatment, and administration of said second treatment resulting in responders to said second treatment and non-responders to said second treatment (page 564 right column and figure 2 and figure 4);

a second pool of study participants comprising non-responders to said first treatment and non-responders to said second treatment, wherein at least one non-responder to said second treatment receives said first treatment and at least one non-

responder to said second treatment receives said second treatment (page 564 right column and figure 2 and figure 4 wherein those patients who are responders or non responders to the double blind placebo lead in are again randomized, therefore at least one participant will be administered active treatment [one non-responder to said second treatment receives said first treatment] and the non responders and responders to placebo in the group without a double blind placebo lead in continue placebo, therefore one participant will continue placebo [at least one non-responder to said second treatment receives said second treatment]); and

an analyzer wherein data from said first treatment and said second treatment are analyzed to provide a determination of effectiveness of said first treatment (page 567 right column and figure 4).

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the computer implemented method of randomization of *Colon* with the various treatment groups of *Faries* since the combination would expedite and insure control of the randomization process allowing for the use of computerized randomization algorithms.

49. **As to claim 26,** see the discussion of claim 25, additionally, *Faries* discloses the system wherein said first treatment corresponds to an active treatment (page 564 Methods section).

50. **As to claim 27,** see the discussion of claim 25, additionally, *Faries* discloses the system wherein said second treatment corresponds to a placebo (page 564 Methods section).

51. **As to claim 28,** see the discussion of claim 25, additionally, *Faries* discloses the system further comprising a second randomizer for receiving information with respect to the non-responders to the second treatment and for randomizing non-responders to said second treatment into a third treatment group and a fourth treatment group (page 564 right column and figure 2 and page 565 left column).

52. **As to claim 30,** see the discussion of claim 29 above, however *Faries* does not discloses means for storing information related to study participants. *Colon* discloses the system further comprising means, coupled to said means for analyzing, for storing information related to the study participants (column 5 lines 25-35 and column 7 lines 66-67 and column 8 lines 1-10).

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify *Faries* with the database of *Colon* since the combination would improve the tracking of trial participants and analysis during the progress of the trial.

Conclusion

53. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

a. "An Issue of Statistic Analysis in Controlled Multi-Centre Studies: How Shall We Weight the Centres?" by Zhengning Lin discusses the use of weighting for statistical analysis in multi-center studies.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Eliza Squires whose telephone number is (571)270-7052. The examiner can normally be reached on Monday through Friday 8 am - 4 pm Eastern Standard Time.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Charles Kyle can be reached on 571-272-6746. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/E. S./
Examiner, Art Unit 4156
9/9/2008

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